UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: May 14, 2020

Subject: Efficacy Review for Advacare 120 Sanitizer Sour, EPA Reg. No. 1677-193
(DP Barcode: 457396, E-Submission: 47703)

From: Kristen Willis, Chief
Product Science Branch
Antimicrobials Division (7510P)

Thru: Thao Pham
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P)
Signed: May 20, 2020

To: Steven Snyderman, Team 33 / Aline Heffernan
Regulatory Management Branch I
Antimicrobials Division (7510P)

Applicant: Ecolab, Inc.
370 Wabasha Street North
St. Paul, MN 55102

Formulation from the Label:

Active Ingredient(s)	% by wt.
Hydrogen peroxide	11.2%
Peroxyacetic acid	15.2%
Other Ingredients	73.6%
Total	100.0%

I BACKGROUND

Product Description (as packaged, as applied): Liquid concentrate

Submission type: Label amendment (A570)

Currently registered efficacy claim(s): laundry disinfectant (bactericidal, virucidal and C. difficile) and laundry sanitizer

Requested action(s): Modify contact time and use concentrations for C. difficile, Enterococcus faecalis-VRE and Carbapenem-resistant Klebsiella pneumoniae (KPC). Bridge claims for treatment of fruit and vegetable process water from EPA Reg. No. 1677-164.

Documents considered in this review:

- Letter from applicant to EPA dated March 6, 2020
- Data Matrix (EPA Form 8570-35) dated March 6, 2020
- Terms of Registration dated April 9, 2020
- 5 efficacy studies (MRID 51076901 - 51076905)
- MRID 46343901 to bridge from EPA Reg. No. 1677-164 reviewed under DP 307171.
- Proposed label dated 04/09/2020 (note revised label was sent via email on 5/6/2020)
- Email from EPA (T. Pham) to Ecolab (B. Peterson) dated 10/3/2019 stating that based on rationale provided by Ecolab, EPA agrees that the 1:5 dilution approach would be reasonable to support revised use-directions for this product (1677-193).
- Email correspondence between EPA (A. Heffernan) and Ecolab (M. Rasinen) dated 5/13/2020 to further clarify the nature of the contaminants noted in MRID 46343903.

II PROPOSED DIRECTIONS FOR USE

"Using the appropriate Ecolab dispenser, inject AdvaCare 120 Sanitizer/Sour into the bleach or rinse step. AdvaCare 120 Sanitizer/Sour is effective in water up to 500 ppm of water hardness (up to 29 grains per gallon). Use AdvaCare 120 Sanitizer/Sour at a rate of 4 to 5 fluid ounces per maximum 60 gallons of water to disinfect a maximum of 100 pounds dry laundry (cwt) according to the use directions below. (119 to 148 mL per maximum 227 L of water to disinfect a maximum of 45 kg dry laundry). Treat the laundry for the required contact time at 140°F to 160°F (60°C to 71°C). Softener can subsequently be added after the disinfecting step. Following the disinfection step, the laundry may be rinsed with water that may include starch, softener, odor neutralizer, fragrance, soil release agent, sour and/or fluid repellent. For further bleaching action, an additional dose of product up to 16 fl. oz./cwt may be added in the bleach or rinse step at a temperature of 90°F to 160°F (32°C to 71°C). Use level, time and temperature will vary depending on stain level, fabric type and load weight. (See list of organisms for required rate of use and heat requirements).

When added as a disinfecting agent at a rate of 5 fluid ounces per 100 pounds of dry laundry at 160°F and laundry is treated for a minimum of 6 minutes, the formulation provides disinfection against:
Enterococcus faecalis-VRE (ATCC 51299)
Carbapenem-resistant *Klebsiella pneumoniae* (ATCC BAA-1705)
[*Clostridioides difficile*, formerly] *Clostridium difficile* (ATCC 43598)
Used as directed, treatment will kill spores of [*Clostridioides difficile*, formerly] *Clostridium difficile* on contaminated [healthcare] laundry and in the laundry wash water."

III AGENCY STANDARDS

Per the EPA approved protocol (1677-193 DP 434653) for laundry disinfection for *C. difficile*, the performance standard is a 6 $\log_{10}$ reduction on 9 fabric test carriers as compared to the control carriers and no growth in the test system water. Three batches of product at the LCL should be tested.

For additional bacteria, 2 batches of product at the nominal concentration should be tested. The performance standard for a laundry disinfectant is no growth in any of the 9 test carriers and 3 wash water subcultures per batch, per test system.

IV STUDY SUMMARIES

1.	**MRID**	51076901	**Study Completion Date:**			02/28/20	
Study Objective		Laundry Disinfectant					
Testing Lab; Lab Study ID		Ecolab Shuman Campus; 2000001					
Test organism(s) ☒ **1** ☐ **2** ☐ **3** ☐ **4+**		*Clostridioides difficile* (ATCC 43598)					
Test Method		Ecolab Microbiological Services SOP MS122-03; *Test Method for Measuring the Sporicidal Efficacy of a Laundry Additive Against Spores of Clostridium difficile on Fabric*					
Application Method		Liquid concentrate					
Test Substance Preparation	**Name/ID**	AdvaCare Disinfectant (Formula code: 984484)					
	Lots ☒ **1** ☐ **2** ☐ **3**	5159JEC200					
	Preparation	Tested concentration: (LCL) 56 ppm of hydrogen peroxide / 75.4 ppm of peroxyacetic acid Dilution: 5 oz/ CWT; 1: 5 fabric to product (75 mL product) Diluent: 500 ppm AOAC synthetic hard water					
Soil load		Yeast extract + Bovine Serum Albumin + Mucin					
Carrier type, # per lot		100% cotton, plain weave 1” x 1.5”- 9 carriers					
Test conditions		**Contact time**	6 minutes	**Temp**	160°F ± 2° F	**RH**	-
Neutralizer for Carriers		0.5% Sodium Thiosulfate + 0.1% Tween 80					
Neutralizer for Wash Water		2% Sodium Thiosulfate + 0.1% Tween 80					
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)		Study was tested according to an Agency reviewed protocol. For one test carrier, 3 contaminant colonies were present on the plate (determined with phase contrast microscopy to be cocci) and were not counted in the CFU/carrier count.					

2.	**MRID**	51076902	**Study Completion Date:**			02/28/20	
Study Objective		Laundry Disinfectant					
Testing Lab; Lab Study ID		Ecolab Shuman Campus; 2000002					
Test organism(s) ☒ **1** ☐ **2** ☐ **3** ☐ **4+**		*Clostridioides difficile* (ATCC 43598)					
Test Method		Ecolab Microbiological Services SOP MS122-03; *Test Method for Measuring the Sporicidal Efficacy of a Laundry Additive Against Spores of Clostridium difficile on Fabric*					
Application Method		Liquid concentrate					
Test Substance Preparation	**Name/ID**	AdvaCare Disinfectant (Formula code: 984484)					
	Lots ☒ **1** ☐ **2** ☐ **3**	3299JE9900					
	Preparation	Tested concentration: (LCL) 55.9 ppm of hydrogen peroxide / 75 ppm of peroxyacetic acid Dilution: 5 oz/ CWT; 1: 5 fabric to product (75 mL product) Diluent: 500 ppm AOAC synthetic hard water					
Soil load		Yeast extract + Bovine Serum Albumin + Mucin					
Carrier type, # per lot		100% cotton, plain weave 1” x 1.5”- 9 carriers					
Test conditions		**Contact time**	6 minutes	**Temp**	160°F ± 2° F	**RH**	-

Neutralizer for Carriers	0.5% Sodium Thiosulfate + 0.1% Tween 80
Neutralizer for Wash Water	2% Sodium Thiosulfate + 0.1% Tween 80
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)	Study was tested according to an Agency reviewed protocol.

3.	**MRID**	51076903	**Study Completion Date:**	02/28/20			
Study Objective		Laundry Disinfectant					
Testing Lab; Lab Study ID		Ecolab Shuman Campus; 2000028					
Test organism(s) ☒ **1** ☐ **2** ☐ **3** ☐ **4+**		*Clostridioides difficile* (ATCC 43598)					
Test Method		Ecolab Microbiological Services SOP MS122-03; *Test Method for Measuring the Sporicidal Efficacy of a Laundry Additive Against Spores of Clostridium difficile on Fabric*					
Application Method		Liquid concentrate					
Test Substance Preparation	**Name/ID**	AdvaCare Disinfectant (Formula code: 984484)					
	Lots ☒ **1** ☐ **2** ☐ **3**	1419JE9400					
	Preparation	Tested concentration: (LCL) 55.3 ppm of hydrogen peroxide / 75.5 ppm of peroxyacetic acid Dilution: 5 oz/ CWT; 1: 5 fabric to product (75 mL product) Diluent: 500 ppm AOAC synthetic hard water					
Soil load		Yeast extract + Bovine Serum Albumin + Mucin					
Carrier type, # per lot		100% cotton, plain weave 1” x 1.5”- 9 carriers					
Test conditions		**Contact time**	6 minutes	**Temp**	160°F ± 2° F	**RH**	-
Neutralizer for Carriers		0.5% Sodium Thiosulfate + 0.1% Tween 80					
Neutralizer for Wash Water		2% Sodium Thiosulfate + 0.1% Tween 80					
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)		Study was tested according to an Agency reviewed protocol. 19 contaminant colonies were present on the plate for the wash water canister and were not counted in the CFU/carrier count. From email correspondence with Ecolab: “Per the raw data for MRID 51076903, the 19 contaminating colonies were described as follows: • Eight colonies were irregular shiny greenish colonies that were cocci under phase contrast microscopy and Gram stained as Gram positive cocci. • Four colonies were irregular tan shiny colonies that were cocci under phase contrast microscopy and Gram stained as Gram positive cocci. • Seven colonies were tiny convex circular dark brown colonies that were irregular rods under phase contrast microscopy. When Gram stained, they were short irregular Gram positive rods without spores. For comparison purposes, the test system on the carrier control numbers plate (the 10^{-5} dilution of replicate 3 was used)					

	showed Gram positive, long straight rods with spores present on the Gram stain as well as under phase contrast microscopy. The typical colony morphology for the test system is circular growth, entire edge, convex, smooth and gray colonies. Based on comparing the cell morphologies via phase contrast microscopy and Gram stain as well as the colony morphology, the 19 colonies were determined to be contamination." In addition, expired lots of neutralizer (for both test carrier and wash water) were used and deemed not to have an impact on the study outcome.

4.	**MRID**	51076904	**Study Completion Date:**			02/27/20	
Study Objective		Laundry Disinfectant					
Testing Lab; Lab Study ID		Ecolab Shuman Campus; 1900125					
Test organism(s) **☒ 1 ☐ 2 ☐ 3 ☐ 4+**		*Enterococcus faecalis-VRE* ATCC 51299					
Test Method		ASTM E2274, Ecolab Microbiological Services SOP MS042-03; Antimicrobial laundry additives					
Application Method		Liquid concentrate					
Test Substance Preparation	**Name/ID**	AdvaCare Disinfectant (Formula code: 984484)					
	Lots **☐ 1 ☒ 2 ☐ 3**	5159JEC200 3299JE9900					
	Preparation	Tested concentration: (LCL) 56 ppm of hydrogen peroxide / 75.4 ppm of peroxyacetic acid (Batch 5159JEC200) 55.9 ppm of hydrogen peroxide / 75 ppm of peroxyacetic acid (Batch 3299JE9900) Dilution: 5 oz/ CWT; 1: 5 fabric to product (75 mL product) Diluent: 500 ppm AOAC synthetic hard water					
Soil load		None					
Carrier type, # per lot		100% cotton, plain weave 1" x 1.5"- 9 carriers					
Test conditions		**Contact time**	5 minutes 45 seconds	**Temp**	160°F ± 2° F	**RH**	-
Neutralizer for Carriers		Letheen Broth + 0.5% Sodium Thiosulfate					
Neutralizer for Wash Water		Letheen Broth + 0.5% Sodium Thiosulfate					
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)		Antibiotic sensitivity report confirmed resistance to vancomycin.					

5.	**MRID**	51076905	**Study Completion Date:**	02/27/20
Study Objective		Laundry Disinfectant		
Testing Lab; Lab Study ID		Ecolab Shuman Campus; 1900126		
Test organism(s) **☒ 1 ☐ 2 ☐ 3 ☐ 4+**		*Klebsiella pneumoniae-KPC* ATCC BAA-1705		

Test Method		ASTM E2274, Ecolab Microbiological Services SOP MS042-03; Antimicrobial laundry additives					
Application Method		Liquid concentrate					
Test Substance Preparation	**Name/ID**	AdvaCare Disinfectant (Formula code: 984484)					
	Lots ☐ **1** ☒ **2** ☐ **3**	5159JEC200 3299JE9900					
	Preparation	Tested concentration: (LCL) 56 ppm of hydrogen peroxide / 75.4 ppm of peroxyacetic acid (Batch 5159JEC200) 55.9 ppm of hydrogen peroxide / 75 ppm of peroxyacetic acid (Batch 3299JE9900) Dilution: 5 oz/ CWT; 1: 5 fabric to product (75 mL product) Diluent: 500 ppm AOAC synthetic hard water					
Soil load		None					
Carrier type, # per lot		100% cotton, plain weave 1” x 1.5”- 9 carriers					
Test conditions		**Contact time**	5 minutes 45 seconds	**Temp**	160°F ± 2° F	**RH**	-
Neutralizer for Carriers		DE Broth					
Neutralizer for Wash Water		DE Broth					
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)		Antibiotic sensitivity report confirmed the stain produces Carbapenamase.					

V STUDY RESULTS

Sporicidal Results – Spores of *Clostridioides difficile* (ATCC 43598)

MRID	51076901-51076903		
6 minute contact time, 1:5 fabric to product ratio, dilution in 500 ppm hard water, 3-part soil load			
Spore purity	Confirmed via phase contrast cell morphology and colony morphology		
Spore qualification	Reported as meeting the criteria of at least a 5-log reduction for the 5,000-ppm NaOCl control, where less than a 3-log reduction is observed for the 1,500 ppm NaOCl control and the numbers control carriers are between 6.0-7.0 logs.		
Batch	5159JEC200	3299JE9900	1419JE9400
Test Date	1/09/20	01/24/20	2/11/20
Spore Titer (spores/mL)	4.5×10^8	4.5×10^8	4.5×10^8
Control Average Log_{10} CFU/carrier	6.11	6.18	6.21
Test Average Log_{10} CFU/carrier	0[a]	0	0
Log reduction for Test Carriers	≥6.11	≥6.18	≥6.21
Mean Log Density per Canister of Wash Water	5.30	5.34	5.15
Mean Log Density of Survivors per Canister of Wash Water	0	0	0[b]

[a] Three colonies were present on one carrier, confirmed to be a contaminant.

[b] Nineteen colonies were present on the filter, but not counted since verified to be contaminants.

Bactericidal results-

MRID	51076904	
Organism	*Enterococcus faecalis-VRE* ATCC 51299	
Conditions	*5 minute 45 seconds contact time, 1:5 fabric to product ratio, dilution in 500 ppm hard water, no soil load*	
Batch	5159JEC200	3299JE9900
Test Date	12/10/19	12/10/19
Control Average CFU/carrier	1.6×10^6	
Control CFU/mL (wash water)	5.0×10^4	
Number of treated fabric carrier tubes exhibiting growth	0/9	0/9
Number of treated wash water tubes exhibiting growth	0/3	0/3

MRID	51076905	
Organism	*Klebsiella pneumoniae-KPC* ATCC BAA-1705	
Conditions	*5 minute 45 seconds contact time, 1:5 fabric to product ratio, dilution in 500 ppm hard water, no soil load*	
Batch	5159JEC200	3299JE9900
Test Date	12/11/19	12/11/19
Control Average CFU/carrier	1.2×10^6	
Control CFU/mL (wash water)	5.4×10^4	
Number of treated fabric carrier tubes exhibiting growth	0/9	0/9
Number of treated wash water tubes exhibiting growth	0/3	0/3

VI STUDY CONCLUSIONS

MRID	Claim	Surface Type	Application Method(s) and Dilution	Contact Time (min)	Soil load	Diluent	Organism(s)	Data support tested conditions?
51076901 51076902 51076903	Laundry Disinfectant, sporicidal	Fabric	Liquid, 1:5 fabric to product ratio	6	3-part soil load	500 ppm hard water	• *Clostridioides difficile* (ATCC 43598)	**Yes**
	Emerging viral pathogen; Enveloped, large and small, non-enveloped viruses							**Yes**
51076904 51076905	Laundry Disinfectant, bactericidal	Fabric	Liquid, 1:5 fabric to product ratio	5.75	no soil load	500 ppm hard water	• *Enterococcus faecalis*-VRE (ATCC 51299) • *Klebsiella pneumoniae*-KPC (ATCC BAA-1705)	**Yes**
46343901*	Treatment of fruit and vegetable process water	Water	Liquid, 2.5-6.7 oz/100 gallons (30 ppm peroxyacetic acid)	1.5	1% vegetable juice	400 ppm hard water	• *Listeria monocytogenes* (ATCC 49594, 191114, 19116) • *Escherichia coli* serotype O157:H7 (ATCC 43895, 35150, 43890) • *Salmonella enterica* (ATCC 10721, ATCC 6962, ATCC 13311)	**No** - Testing was not conducted at the LCL

* MRID 46343901 was reviewed under EPA Reg. No. 1677-164 (DP 307171). Tested was conducted for 3 batches of product and acceptable efficacy was demonstrated. Based on the formulation for the reference product it would support bridging to the subject product (1677-193) however testing was not conducted at LCL.

VII LABEL COMMENTS

Label Date: 04/09/2020

1. The proposed label claims that the product, AdvaCare 120 Sanitizer/Sour, when diluted at 5 fl oz. per 60 gallons of 500 ppm hard water per 100 lbs of dry laundry, is an effective disinfectant against the following on precleaned textiles (during the rinse step)for a 6-minute contact time:

   Clostridioides difficile (ATCC 43598)
   Enterococcus faecalis-VRE (ATCC 51299)
   Klebsiella pneumoniae-KPC (ATCC BAA-1705)

   These claims are **acceptable** as they are supported by the submitted data.

2. The proposed label claims that the product, AdvaCare 120 Sanitizer/Sour, when diluted at 2.5-6.7 fl oz. per 100 gallons (30-80 ppm peroxyacetic acid) of process water for a 1.5-minute contact time, is effective at reducing the following pathogens in process (reuse) water holding systems, and equipment holding (process) (reuse) water:

   Listeria monocytogenes
   Escherichia coli O157:H7
   Salmonella enterica

   These claims are **not acceptable** as they are not supported by the submitted data. Testing was not conducted at the LCL.
   - The registrant may choose to revise the directions for use to specify a minimum of 4 fl oz per 100 gallons. The data would support this dilution.

3. The proposed label claims that the product, AdvaCare 120 Sanitizer/Sour, qualifies for the following emerging viral pathogens claims as described in the letter from the applicant to EPA dated April 9, 2020:

For an emerging viral pathogen that is a/an…	*…follow the directions for use for the following organisms on the label:*
Enveloped virus	*Clostridioides difficile* (ATCC 43598)
Large, non-enveloped virus	*Clostridioides difficile* (ATCC 43598)
Small, non-enveloped virus	*Clostridioides difficile* (ATCC 43598)

These claims are **acceptable** as they are supported by the cited data. AdvaCare 120 Sanitizer/Sour is an EPA registered disinfectant with claims for a spore forming organism, *C. difficile.* Spores are the most difficult form of microorganism to kill according to the hierarchy of microorganisms and their resistance to disinfectants. As such, this product when used according to the directions for use for *C. difficile* is expected to inactivate all types of emerging viruses.

Revise the following statement under the Emerging Viral Pathogens table on page 9 to exactly match the following. <u>Also revise the "Terms of Registration as applicable</u>:

"[Advacare 120 Sanitizer/Sour] has demonstrated effectiveness against Clostridioides difficile, a spore forming organism, on laundered [fabric] [linen]. Spores are the most difficult form of microorganism to kill according to the hierarchy of microorganisms and their resistance to disinfectants. Therefore, [Advacare 120 Sanitizer/Sour] can be used against [name of emerging virus] when used in accordance with the directions for use against Clostridioides difficile when added as a disinfecting agent at a rate of 5 fluid ounces per 100 pounds of dry laundry at 160°F and laundry is treated for a minimum of 6 minutes. Refer to the [CDC] [OIE] website at [insert pathogen-specific website address] for additional information."

4. Make the following changes to the proposed label:
   a. On page 4 of the proposed label,
      - Remove the directions for Pathogen Reduction and Control in (Industrial) (Process) (Reuse) (Holding) Waters In Laundry Facilities or revise the use rate per item 2 above.

   b. On page 6 of the proposed label,
      - remove "attacks" as this may be misleading regarding the activity of the product.
      - Remove "EPA approved [method] process" as this may imply agency endorsement.
   c. On page 7 of the proposed label,
      - Remove "EPA registered" from the claim "A comprehensive [EPA] registered laundry [oxidizer] [disinfectant] concentrate available for [contaminated] [healthcare] [and] [food processing] textiles"

   d. On pages 6-8 of the proposed label,
      - Further clarify "reusable masks". Specify fabric masks to differentiate them from other types of masks not meant to be laundered.

   e. On page 7 of the proposed label,
      - Remove "[EPA] registered" as this language on the label may imply agency endorsement.
      - Remove "[than the CDC and HICPAC 2003 recommendation (guideline) for processing healthcare linens]". References to guidance by federal agencies should be informative, not comparative.
      - Each instance of "antibiotic resistant bacteria" or "superbug" should be linked to the relevant organisms. Qualifying organisms should not be optional language.

   f. On page 8 of the label, remove "Personal Protective Equipment (PPE)" or qualify with specific fabric equipment.